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DOI: <https://doi.org/10.1093/cid/cis850>

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ZORA URL: <https://doi.org/10.5167/uzh-69254>

Journal Article

Published Version

Originally published at:

Bosshard, Philipp P; Graf, Nicole; Knaute, Damaris Fröhlich; Kündig, Thomas; Lautenschlager, Stephan; Weber, Rainer (2013). Response of treponema pallidum particle agglutination test titers to treatment of syphilis. *Clinical Infectious Diseases*, 56(3):463-464.

DOI: <https://doi.org/10.1093/cid/cis850>

Correspondence

Response of *Treponema pallidum* Particle Agglutination Test Titers to Treatment of Syphilis

TO THE EDITOR—We recently published on the serological response to treatment of syphilis according to disease stage and human immunodeficiency virus (HIV) status [1]. In particular, we analyzed the course of the Venereal Disease Research Laboratory (VDRL) and a specific immunoglobulin M capture enzyme-linked immunosorbent assay test (Pathozyme-IgM) in 264 patients. Syphilis disease stage significantly influenced treatment response whereas HIV coinfection had an impact only in patients with primary syphilis.

Because not much is known about the response of the widely used *Treponema pallidum* particle agglutination (TPPA) test titer to syphilis treatment, we also analyzed the TPPA (Fujirebio, Tokyo, Japan) results. A total of 212 patients with an initially positive TPPA test (titer $\geq 1:80$) were followed for at least 6 months after treatment and had at least 3 follow-up serologies.

On average, a reduction of 3.3 dilution steps in the TPPA titer was observed during a mean follow-up duration of 429 days (Table 1). However, only 117 (55%) patients showed a continuous decrease of the TPPA titer, 30 (14%) maintained a constant titer, 4 (2%) had an increasing titer, and, most interestingly, 61 (29%) patients demonstrated a ≥ 2 dilution steps (≥ 4 -fold) fluctuating titer—that is, the titer some when during follow-up increased at least 4-fold with subsequent decrease to the baseline or a lower titer. In 17 of these patients the intermittent increase was even ≥ 4 dilution steps. There was no

association with HIV status ($P = .117$). None of the patients had clinical evidence for reinfection or by VDRL serology. We therefore conclude that a 4-fold or greater increase of the TPPA titer without other serological (eg, VDRL) or clinical evidence does not necessarily indicate syphilis reinfection.

A second interesting observation was that 28 of 212 (13%) patients showed seroreversion of the TPPA (Table 1). Seroreversion was defined as the last

follow-up serum being nonreactive. In 20 of these patients, >1 follow-up serum (up to 5) was nonreactive. The median time to seroreversion was only 227 days. Half (14 of 28) of the patients had relatively high initial titers of $\geq 1:1280$. Seroreversion was associated with HIV coinfection ($P = .004$), especially in secondary syphilis where 10 of 11 patients were HIV positive. Although described earlier [2–6], it is not widely known among clinical and laboratory staff that

Table 1. Characteristics and *Treponema pallidum* Particle Agglutination Test Results of 212 Patients Who Were Followed for at Least 6 Months

Characteristic	All Patients (N = 212)	TPPA Seroreversion (n = 28)	P Value ^a
Stage of syphilis			.06 ^b
Primary	74	16 (22)	
Secondary	105	11 (10)	
Tertiary	6	0	
Latent	27	1 (4)	
HIV serostatus			.004 ^b
Positive	95	20 (21)	
Negative	117	8 (7)	
TPPA baseline titer			
Median titer	1:10240	1:960	<.001 ^c
Interquartile range	1:1280–1:40960	1:160–1:3200	
TPPA follow-up titers			
Mean decrease (dilution steps)	3.3	5.0	.001 ^d
Patients with ≥ 4 -fold constant decrease	117 (55)	NA	
Patients with ≥ 4 -fold fluctuating titer	61 (29)	NA	
Patients with constant titer (± 1 titer)	30 (14)	NA	
Patients with ≥ 4 -fold increasing titer	4 (2)	NA	
Duration of follow-up, d, mean (range)	429 (175–729)	491 (223–711)	.274 ^d
Duration until seroreversion, d, mean (range)	NA	227 (101–656)	
No. of follow-up visits, mean (range)	4.6 (3–12)	4.8 (3–8)	.139 ^c

Data are presented as No. (%) unless otherwise specified.

Abbreviations: HIV, human immunodeficiency virus; NA, not applicable; TPPA, *Treponema pallidum* particle agglutination.

^a As compared with the subgroup without seroreversion.

^b Fisher exact test.

^c Exact Mann-Whitney test.

^d *t* test.

this may occur. It is generally believed that the TPPA remains positive after treatment. The overall rate of 21% HIV-coinfected patients with TPPA seroreversion, for unknown reasons, is higher than the previously reported rates of 5%–11.5% [2–5]. Additionally, we found 7% HIV-negative patients with TPPA seroreversion. Only 2 previous studies reported seroreversion among HIV-negative patients with rates of 3%–13% [2, 6]; other studies did not find reversion among HIV-negative persons [3–5].

In conclusion, a 4-fold or greater increase of the TPPA titer does not necessarily indicate reinfection or inadequate therapy, and a negative TPPA titer does not exclude previous syphilis infection.

Note

Potential conflicts of interests. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Clinical Infectious Diseases **2013;56(3):463–4**

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DOI: 10.1093/cid/cis850